

REMARKS

After entry of this Amendment, claims 19 and 21-38 will be pending. Claim 20 and 30 are cancelled in this Amendment. Claims 26 and 28 are allowed. Claims 19, 21, 23-25, 27, 29, 31-35, and 37-38 are under examination.

Applicants filed an Amendment and Notice of Appeal on May 10, 2004. An Advisory Action was mailed on May 24, 2004. The Advisory Action states that the Amendment filed May 10, 2004 was not entered. The below response takes into account the rejections raised in the January 8, 2004 Office Action and the Advisory Action.

Rejections Under 35 U.S.C. §112, First Paragraph

Claims 19, 21-25, 27 and 29-38 have been rejected for failing to comply with the written description requirement.

With respect to claims 19, 21, 29 and 35, and the claims dependent therefrom, the Examiner states that the specification demonstrates possession of a variant nucleic acid with a G at position 3949, but does not demonstrate possession of a variant with A or C at that position, or the effect of having an A or C at that position. The Examiner further alleges that "with the exception of SEQ ID NO:1 with a T or a G at position 3949, the skilled artisan cannot envision the detailed chemical structure" of the oligonucleotides encompassed by the claims. The Examiner further states that the specification does not teach that either the C or the A allele occur n nature and does not set forth the effect of such a polymorphism in either thrombospondin activity or disease association.

Applicants respectfully traverse. To satisfy the written description requirement, the description of the invention must allow a person of skill in the art to recognize that the applicant invented and was in possession of what is claimed. *See, e.g., Noelle v. Lederman*, 69 U.S.P.Q.2d 1508, 1513 (Fed. Cir. 2004). As acknowledged by the Examiner, an applicant can show possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention.

Claim 19 and 29 have been amended to recite nucleic acids comprising reciting guanine (G) at position 3949 of SEQ ID NO:1. Therefore, this rejection with respect to claims 19 and 29 has been obviated.

Claims 21 and 35, and the claims dependent therefrom, recite oligonucleotides that hybridize under stringent conditions to a nucleic acid molecule comprising nucleotide position 3949 of SEQ ID NO:1 wherein the nucleotide at position 3949 is a nucleotide other than thymidine (T). As it is well known in the art, there are typically three nucleotides other than T: A, C and G. Therefore, the claims include oligonucleotides which hybridize under stringent conditions to a nucleic acid molecule comprising A, C or G at position 3949 of SEQ ID NO:1.

It is clear that Applicants envisioned such a molecule by their statement that the nucleotide at this position must be a nucleotide other than T. Therefore, a person of skill in the art reading the specification would have understood that the Applicants were in possession of the claimed invention at the time the application was filed. Accordingly, Applicants respectfully submit that the specification provides adequate description for the instant claims. Further, the oligonucleotides of claims 21 and 35 can be used to distinguish sequences which have a G at position 3949 of SEQ ID NO:1, from molecules that have a T at that position for use in, i.e., diagnostic procedures. Therefore, Applicants respectfully submit that claims 21 and 35, are the claims dependent therefrom comply with the requirements of 35 U.S.C. §112, first paragraph.

With respect to claims 21 and 35, and the claims dependent therefrom, the Examiner states that the claims encompass mutants, variants and homologs of SEQ ID NO:1 which were not described in the specification. Further, the Examiner states that the claims encompass sequences that hybridize to regions of SEQ ID NO:1 that do not comprise position 3949. Claims 21 and 35 have been amended to require the claimed allele-specific oligonucleotide comprise more than 10 contiguous nucleotides, wherein said oligonucleotide hybridizes under stringent conditions to a nucleic acid molecule comprising nucleotide position 3949 of SEQ ID NO:1 and wherein said allele-specific oligonucleotide hybridizes to said nucleic acid molecule at a region which encompasses nucleotide position 3949. Thus, the claims, as amended, do not encompass unrelated nucleotide sequences that can hybridize to SEQ ID NO:1 as suggested by the Examiner.

In the Advisory Action, the Examiner objected to the recitation of “stringent conditions” under 35 U.S.C. § 112, 1. Applicants respectfully traverse. The specification states (p.10; *emphasis added*):

Hybridizations are usually performed under *stringent conditions*, for example, at a salt concentration of no more than 1 M and a temperature of at least 25C. For example, conditions of 5X SSPE (750 mM NaCl, 50 mM NaPhosphate, 5 mM EDTA, pH 7.4) and a temperature of 25-30C, or equivalent conditions, are suitable for allele-specific probe hybridizations. Equivalent conditions can be determined by varying one or more of the parameters given as an example, as known in the art, while maintaining a similar degree of identity or similarity between the target nucleotide sequence and the primer or probe used.

Thus, the term “stringent conditions” is supported in the specification and is well understood by a person having ordinary skill in the art. Applicants respectfully submit that the recitation of “stringent conditions” does not render the claims indefinite.

With respect to claim 29, and the claims dependent therefrom, the Examiner objects to the claim language “consisting of a portion of at least 10 contiguous nucleotides of SEQ ID NO:1.” With respect to claim 29, and the claims dependent therefrom, Applicants note that the claims, as amended, no longer recite the objected to language.

In view of the arguments presented above, Applicants respectfully request reconsideration and withdrawal of the written description rejections.

Rejections Under 35 U.S.C. §112, Second Paragraph

Claims 29-34 have been rejected as indefinite. The Examiner states that the recitation of “consisting of a portion of at least 10 contiguous nucleotides of SEQ ID NO:1 …” is indefinite. Applicants have amended the claims such that they no longer recite the objected to language. Accordingly, the Examiner’s rejection has been rendered moot.

In the Advisory Action, the Examiner acknowledges that the proposed amendment to claim 29 would overcome the rejection made under 35 USC § 112, second paragraph in the January 8, 2004 Office Action.

Rejections Under 35 U.S.C. §102

Kazuno

Claims 21-24 are rejected under 35 U.S.C. §102(b) as being anticipated by Kazuno et al., *Euro. J. Cancer* 35:502-506 (1999) (“Kazuno”). The Examiner alleges that Kazuno teaches primers “which are capable of hybridizing to SEQ ID NO:1 wherein the nucleotide at position 3949 is a nucleotide other than thymidine.”

Applicants respectfully traverse. Claims 21-24, as amended, recite an allele-specific oligonucleotide which hybridizes at a region which encompasses nucleotide position 3949 of SEQ ID NO:1. The primers disclosed by Kazuno do not hybridize at a region which encompasses nucleotide position 3949 of SEQ ID NO:1, as recited by amended claims 21-24. Rather, Kazuno teaches primers which hybridize to a different portion of SEQ ID NO:1. Accordingly, Applicants request that the Examiner withdraw this rejection.

GenBank Accession No. AF109906

Claims 29-34 are rejected under 35 U.S.C. §102(b) as anticipated by GenBank Accession No. AF109906. The Examiner alleges that the cited reference teaches a sequence “that contains a sequence complementary to positions 3940-3954 of SEQ ID NO:1 wherein position 3949 is a G.”

Applicants respectfully traverse this rejection. Claim 29 recites an isolated nucleic acid molecule consisting of more than 10 contiguous nucleotides of SEQ ID NO:1. The cited GenBank Accession No. does not contain a sequence consisting of more than 10 contiguous nucleotides of SEQ ID NO:1. The transitional phrase “consisting of” is closed language and excludes any element, step, or ingredient not specified in the claim. See MPEP § 2111.03. Therefore claim 29 excludes any nucleic acid molecule which includes a nucleotide sequence not included within SEQ ID NO:1. The cited GenBank Accession No. discloses a mouse

sequence corresponding to a mouse MHC class III region RD gene which comprises 15 contiguous nucleotides of SEQ ID NO:1 as part of a larger sequence that further comprises sequences which are not present in SEQ ID NO:1. Thus, the sequence disclosed in the cited GenBank Accession No. does not meet each and every limitation of the claim and therefore does not anticipate claim 29 and the claims dependent thereon. Accordingly, Applicants request that the Examiner withdraw this rejection.

Fodor and Brennan

Claims 21-24, 29-30, and 35-38 are rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 6,582,908 to Fodor et al. (“Fodor”). According to the Examiner, Fodor teaches an array of all possible 10mers. The Examiner concludes that the nucleic acids of the instant application read on the isolated nucleic acids of Fodor.

Claims 29 and 30 are rejected under 35 U.S.C. §102(e) as anticipated by U.S. Patent No. 5,474,796 to Brennan (“Brennan”). According to the Examiner, Brennan teaches an array of all possible 3mer isolated nucleic acids. The Examiner concludes that the claims of Brennan encompass the sequence CGC which is taught by Brennan.

Applicants respectfully traverse. Neither Fodor nor Brennan discloses a nucleic acid sequence that meets all of the limitations of the cited claims. Specifically, neither Fodor nor Brennan discloses an oligonucleotide comprising more than 10 nucleotides which hybridizes nucleotide position 3949 of SEQ ID NO:1 (as required by claims 21 and 35), or an oligonucleotide comprising more than 10 nucleotides and comprising nucleotide position 3949 of SEQ ID NO:1 (as required by claim 29).

Anticipation requires that each and every limitation of the claim is disclosed in the prior art. In this case, the prior art does not disclose oligonucleotides having more than 10 nucleotides. Further the prior art provides only a general teaching of an infinite number of 10mers or 3mers containing any sequence. The specific oligonucleotides and arrays of the instant claims are not specifically disclosed or suggested by the prior art.

Accordingly, claims 21-24, 29-30, and 35-38 are not anticipated by Fodor or Brennan. Reconsideration and withdrawal of these anticipation rejections are respectfully requested.

Rejections Under 35 U.S.C. §103

Claims 35-38 have been rejected under 35 U.S.C. §103 as anticipated over Kazuno in view of Brennan. According to the Examiner, Kazuno teaches primers which are capable of hybridizing to SEQ ID NO:1 wherein the nucleotide at position 3949 is a nucleotide other than thymidine, and Brennan teaches placing sequences on an array for the purposes of detecting target oligonucleotides.

Applicants respectfully traverse this rejection. In order for a combination of references to render a claimed invention obvious, the prior art references must teach or suggest all of the claim limitations. In this case, Kazuno and Brennan, either alone or in combination, do not teach all of the limitations of claims 35-38.

Claim 35 recites an array comprising an allele-specific oligonucleotide comprising more than 10 nucleotides contiguous nucleotides which hybridizes to nucleotide position 3949 of SEQ ID NO:1. As discussed above, Kazuno does not disclose a primer which hybridizes to a nucleotide position 3949 of SEQ ID NO:1 of SEQ ID NO:1. Brennan does not cure this deficiency. Therefore, for at least this reason, the combination of Kazuno and Brennan does not teach or suggest the invention of claims 35-38. Accordingly, Applicants respectfully request that the Examiner withdraw this rejection.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call Lisa M. Treannie at (617) 951-7725 or the undersigned.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 18-1945, from which the undersigned is authorized to draw, under Order No. WIBL-P01-575.

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Respectfully submitted,

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